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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,006	08/24/2000	Patrick Tso	10738-17	5310

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EXAMINER	
MITRA, RITA	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/623,006	TSO ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-14,19 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-14, 19, 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The request filed on January 3, 2005 for a re-consideration based on the declaration under 37 C.F.R. 1.132 is acknowledged. An action on the request follows.

Status of the Claims

Applicants' amendment and response to office action dated June 30, 2004, filed on January 3 2005, is acknowledged. No claim is amended. Claims 2, 3, 15-18 and 20-62 have been canceled. Therefore, claims 1, 4-14, 19 and 63 are currently pending and are under examination.

Response to Remarks and Arguments

Rejection of claims 1, 4-14, 19 under **35 U.S.C. § 102** is withdrawn in view of the Declaration under 37 C.F.R. 1.132

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-14, 19 and 63 stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 4, 13, 14 and 63 encompass the subject matter that is not defined in the specification. The claims are directed to a method for inhibiting lipid oxidation associated with a

condition in a patient, comprising administering to a patient a composition comprising a pharmacologically effective amount of an apolipoprotein (apo) A-IV peptide or derivative, analog, homolog, or fragment thereof, to inhibit lipid oxidation. Additionally the claimed invention assert that the apolipoprotein A-IV is a peptide sequence of from 6-71 amino acids in length and wherein the peptide or derivative, analog, homolog, or fragment thereof has substantially the same lipid oxidation properties as the apolipoprotein A-IV molecule, however, the specification, only discloses cursory conclusions (see page 6, lines 3-6), without data to support the findings, which state that a number of novel lipid oxidation suppressant peptides, derived from apolipoprotein A-IV, have been made, these peptides possess lipid oxidation inhibiting properties which when administered orally or intravenously, can be used to decrease atherosclerosis. The specification at pages 6-9 and 12-15 provide a limited discussion of the derivative, analog, homolog or fragment. As it is stated at page 12 that the invention provides for a number of lipid oxidation inhibiting peptides of approximately 5-90 amino acids in length, which substantially correspond in sequence to amino acid sequence found in specific portions of apo AIV, which is insufficient description as no characteristics are provided nor any evidence to demonstrate retention of function with regard to inhibitory activity in lipid oxidation. Moreover based on open language "comprising", the claimed apolipoprotein can have sequences added to the N-terminal or C-terminal end and any polypeptide or peptide, having an undefined structure.

Claim 4 is directed to the method of claim 1, wherein the peptide has an amino acid sequence comprising amino acid sequence set forth in SEQ ID NO: 5 or a derivative, analog, homolog or fragment of the said sequence. However, the specification provides only a generic description of how a variety of derivative, analog, homolog or fragment can be generated (page 22-26), no specific guidance is provided on the generation of the derivative, analog, homolog or fragment that demonstrate the biological activity of the peptide sequence of SEQ ID NO: 5. However the specification lacks adequate written description to demonstrate to a skilled artisan that applicant was in possession of the claimed invention.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the apolipoprotein AIV, which comprises derivative, analog, homolog or fragment, which have substantially the same lipid oxidation properties as the apolipoprotein AIV wild-type molecule. Furthermore, there is no written description of either a representative number of the

variants or of a common structural feature of the apo AIV wild-type which encompasses all the variants.

In response Applicants traverse the rejection (see page 6). The reason for the traversal is the apolipoprotein A-IV peptide is from 6-71 amino acids in length and the peptide or derivative or analog, homolog or fragment thereof has substantially the same lipid oxidation properties as the apolipoprotein A-IV molecule. Applicants' arguments have been fully considered but not found persuasive because the specification at pages 6-9 and 12-15 provide a limited discussion of the derivative, analog, homolog or fragment. As it is stated at page 12 that the invention provides for a number of lipid oxidation inhibiting peptides of approximately 5-90 amino acids in length, which substantially correspond in sequence to amino acid sequence found in specific portions of apo AIV, which is insufficient description as no characteristics are provided nor any evidence to demonstrate retention of function with regard to inhibitory activity in lipid oxidation.

Applicants urge at page 6, last paragraph that the specification at page 6, paragraph 2 clearly teaches that the inventive peptides contemplated for use in the present methods comprise at least a six amino acid sequence derived from the amino terminal portion of the mature apolipoprotein A-IV molecule, also larger peptides of 15 and 90 amino acids, each containing within its sequence the aforementioned repeat sequence are also contemplated by the present invention. However, the specification fails to define the specific position of the N-terminal portion of the mature apolipoprotein from where said six amino acid sequence is derived and also no function of this derivative has been provided.

Further Applicants assert at page 7 last paragraph that an analog might comprise a peptide having substantially identical amino acid sequence to a peptide provided herein as SEQ ID NO: 1-13 and in which one or more amino acid residues have been conservatively substituted with chemically similar amino acids. The specification provides only a generic description of how a variety of derivatives can be generated, no specific information is provided on the generation of the derivatives that demonstrate the biological activity of the apolipoprotein A-IV.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given

protein the positions within the protein's sequence where such amino acid substitution can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding the active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitution or no substitutions. However, the specification provides no description of the positions in the protein, which are tolerant to change (e.g. by amino acid substitutions or deletions, insertion or/and addition), and the nature and extent of changes that can be made in these positions. Therefore, the skilled artisan cannot envision the detailed chemical structure of the apolipoprotein derivatives analogs homologs and fragments, thus, claims reciting said derivatives analogs homologs and fragments lack adequate written description.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

No claim is allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Jon Weber, can be reached at (571) 272-0925. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0547.

Rita Mitra, Ph.D.
March 20, 2005

JON WEBER
SUPERVISORY PATENT EXAMINER